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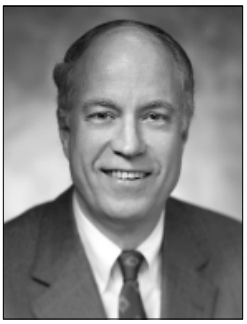

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SALT AND BLOOD PRESSURE

A number of years ago, I covered my food with a heavy dose of salt before taking a single bite. After a while, my blood pressure began to rise, and I considered how foolish I was to add salt to my food at the table. I stopped adding salt abruptly, and within a month or so I found that I did not miss the added salt one iota and, indeed, I believe I enjoyed the food more.

Unfortunately, salt added at the table accounts for only 15% of the salt most Americans consume. Most of the salt is hidden in processed food, which now accounts for about 80% of our salt intake. Why is it that salt, which is so beneficial as a preservative and has been added to food for thousands of years, should only in recent years be discovered to be so harmful? In 1998, MacGregor and de Wardener published a book entitled *Salt, Diet and Health: Neptune's Poisoned Chalice: The Origins of High Blood Pressure* (1). The book traces the fascinating story of how humans became addicted to salt, its past economic and historical importance, and the recent realization that salt is responsible for a great number of deaths throughout the world. Unfortunately, it is difficult to reverse the present state of affairs in all Western countries unless we avoid most processed foods. It would be much easier if the food industry could be persuaded to stop adding such unnecessarily large amounts of salt to foods such as bread, breakfast cereals, and prepared meals. For purely commercial reasons, the food industry opposes the now overwhelming evidence that relates salt intake to the development of high blood pressure.

Salt, of course, means sodium chloride, as used in cooking and on the roads in winter. Salt is made up of 40% sodium and 60% chloride. For 5 million years, according to MacGregor and de Wardener, our ancestors added no salt to their diet. Nowadays, such a diet would be considered very low in salt. This was the diet of all mammals during evolution, and they were fairly adapted to it. Humans, like other mammals, relied on the small amounts of salt naturally present in food to regulate the amount of fluid in the body. Very powerful mechanisms for conserving salt within the body were developed.

The addition of salt to food began relatively recently, about 5000 years ago. As people became increasingly addicted to it, salt became the most important object of trade and the economic foundation of several empires. It was used by authoritarian governments to control their people and as the main source of tax revenue.

Our consumption of salt today is 10 to 20 times greater than it was 5000 years ago. Because the human body had become geared to conserve salt, it found it difficult to dispose of this relatively sudden, in evolutionary terms, increase in salt intake. The result was a general rise in blood pressure. Those who had the greatest difficulty getting rid of the excess salt had the greatest rise. A rise in blood pressure, of course, damages the arteries, and hypertension is the major cause of stroke and a major contributor to heart disease.

Salt in the diet from Paleolithic times to the present: Until 4 to 8 million years ago, fruit was the main component of mammals' diet. Later, when the human and ape lines diverged, the human line began to eat a modest amount of meat until 1.6 to 1.8 million years ago, when *Homo erectus* began to consume more meat. These hunter-gatherers lived in areas where there were large numbers of grazing animals. Their tools were used principally to process the game caught. Eventually, their diet consisted of 50% meat and 50% plants. If it is assumed that the content of the minerals in the wild animals our ancestors hunted was the same as in present-day cows and sheep, the daily intake of salt in Paleolithic times was <1 g of salt per day. Because of the large consumption of vegetables and fruit, the potassium content of the diet then was 16 times greater than the salt intake. Potassium, in contrast to salt, lowers blood pressure. In comparison to our hunter-gatherer ancestors, salt intake is now about 10 times greater, while potassium intake is considerably less than that of salt.

The consumption of salt began to rise about 5000 to 10,000 years ago, when the combined effects of overhunting, climate changes, and particularly population growth led to a wave of agriculture creeping across Europe at a rate of about 1 km a year. That salt intake increased at this time is suggested by the observation that languages before Greek and Sanskrit—the older of the Indo-European languages—had no word for salt. During the first few thousand years after the advent of agriculture, the intake of meat declined, and the proportion of vegetables in the diet increased by up to 90%. It is not clear why the increase in salt intake appeared as the spread of agriculture occurred. Some suggest that these early farmers consumed as much salt as their hunter-gatherer ancestors did.

Probably the most important factor that increased salt intake was salt's magical property of preserving food. Since farmers were tied to their fields, it was much more difficult for them to acquire fresh meat. They also had to preserve food during the winter for their survival. Preservation was achieved by soaking meat in brine. Salt permeates food and makes bacterial life impossible. Although it is not known when it started, salt preservation was

used in Egypt by at least 2000 BC. It is now known that highly salted food suppresses the salt taste buds in the mouth so that natural foods become insipid and unappetizing. As a result, salt would have to be added to fresh food to make it as appetizing as preserved food.

The addiction for salt also must have been exacerbated by its increasing availability. The change from a nomadic to an agricultural way of life gave rise, of course, to settled communities, between which trade began to flourish. Salt became a precious article of commerce. About 1000 years ago, salt intake in the Western world had risen to about 5 g per day. It continued to rise until the 19th century when, in Europe, it was about 18 g per day. In the 16th century in Sweden, when there was a high consumption of salted fish, it has been calculated that the daily salt intake rose to 100 g per day. A worldwide reduction of salt intake to an average of 10 g per day during the 20th century was probably due to the introduction of refrigeration.

Salt intake in isolated tribes and in chimpanzees: There are numerous small populations, scattered throughout the world, which because of their isolation recently ate or continue to eat a low-salt diet. The salt intake of these isolated tribes varies from an average of about 0.05 to 2 g per day. There is no indication that they are less healthy than populations who consume an average of 10 g per day and, on the contrary, there is evidence that they are more fit and have less cardiovascular disease. Numidian nomads and certain Bedouins who feed on fish and roasted meat never eat salt with food. The Bedouins think that it is ridiculous to do so. Eskimos who have not been in contact with Western civilization had a strong dislike for salt and would even avoid food in which saltiness could be detected.

Addiction to salt has been introduced subsequently to many of these isolated tribes and, furthermore, in a colony of chimpanzees. Under normal circumstances, chimpanzees eat a diet of vegetables and fruits, which has a low salt and high potassium content. However, for many years, a colony of chimpanzees in San Antonio, Texas, was daily fed 1 to 2 kg of biscuits that had been specifically manufactured for monkeys. These biscuits provided a salt intake of 6 to 12 g per day—under the assumption that the average human intake of 10 g was appropriate for humans' nearest phylogenetic relative. The biscuits also provided an appropriate potassium intake of 6 to 11 g daily. The chimpanzees then were given biscuits identical to the original ones except for their low salt content (0.5 g per day). They refused the low-salt biscuits and rapidly lost weight. Thus, these chimpanzees had become so addicted to the taste of high-salt biscuits that they found the taste of low-salt biscuits so repellent that they preferred to do without.

Herbivores may suffer from salt deficiency and will travel miles to salt licks. In contrast, carnivores come to salt licks to eat the herbivorous animals and not the salt. The aversion for salt exhibited by low-salt–eating populations demonstrates that humans have no innate liking for salt and that, on the contrary, hedonism for salt is an acquired characteristic, a state of salt addiction for an intake far exceeding physiologic requirements.

Physiologic needs and cultural addiction: In 1853, Lehmann, a physiologist, asserted that humans had no need to add salt to natural food (1). He had been led to this opinion by noting that most animals do well on natural food without the addition of salt. He admitted that some herbivores (e.g., cows and deer) ate salt eagerly when they were offered it or when they came across it in salt licks, but he believed that there was no proof that they needed it. At the time, Lehmann was a voice crying in the wilderness, but today most veterinarians have similar views.

Cultural addiction to a high salt intake in modern humans is induced early in life. Infants are either indifferent to or avoid moderate to high concentrations of salt, but by 2 or 3 years of age, children commonly prefer salt on their food. It appears that the ability to taste salt develops after 4 months of life. It is uncertain whether this preference for salt develops because of maturation in infants' abilities to detect salt, which they then find pleasurable, or whether, as is more probable, the normal high salt content of food given to children conditions them to its taste. Some investigators have reported that a preference for salty food in infants can be induced by only one exposure to the salted food. It is hardly surprising, therefore, that as these children get older, their addiction fanned by commerce, they crave salty foods avidly.

Assertions about cravings in children were affirmed in 1986. Urinary salt excretion (virtually all the salt consumed is excreted in the urine) was measured in 4- to 6-year-old children in a study in the United Kingdom (1). The mean weight of the children was 21 kg, and the mean 24-hour salt excretion was 4 g. Although it is difficult to compare salt excretion in young children with that of adults, when such excretion was compared for an equivalent muscle mass, it was 3.5 times greater in the children than the average excretion in adults, which is indicative of an enormous intake.

A revered substance: The importance of salt in purifying and preserving food raised it from being a mere chemical that was dug from the ground or recovered from the sea to a revered substance, the qualities of which far exceeded its natural properties. Salt in some cultures was used to ward off the evil eye, since it was believed that the devil was afraid of salt.

The Romans considered salt to be a sacred article of food, and it was a matter of religious principle with them to see that salt was the first item placed on the table and the last item removed from it. The saltcellar was seen as a symbol of friendship and hospitality, a sign that the guest had been invited in love and that, as the salt remained on the table after other articles had been removed, friendship was perpetual even if feasts and meals came to an end. Over the years, the emblematic saltcellar increasingly became a decorative piece. The rank of guests at a banquet in England was indicated by their place at table with reference to the saltcellar, which was in the center.

Salt was perceived to constitute the essence of things, particularly of life itself. Christ told his disciples, "Ye are the salt of the earth," i.e., the best of the human race. Referring to them, he asks, "If the salt has lost its savour wherewith shall it be salted?" Comparing them to salt, which was thought to lose its saltiness if exposed to the sun, Christ was questioning how the disciples might be restored if they fell from grace. Sometimes salt was thought to be the "soul" within the body.

Salt rapidly moved from the magical to the medicinal. Salt was used extensively throughout history to prevent and cure certain diseases. It was thought that the corruption of a corpse in the grave was due in part to worms and that salt delayed this

corruption. Salt, therefore, was used to treat the living who suffered from worms.

Salt also was considered to be a symbol of procreation. Because of its saltiness, the sea was believed to be a fructifying creative element, with its wealth of fish. It was thought that feeding a dog salt increased the number of puppies and that carrying salt on ships led to a greater multiplication of mice. Salt was both connected with barrenness—presumably because an excess of salt prevents all growth in deserts and other places—and used by women to prevent barrenness. The dread of impotence on the marriage night (an embarrassment known at one time as the "ligature") could be allayed if one or both partners carried some salt in their pockets or on their clothes or the wife had salt in her shoe. Now that it is known that a sudden increase in salt intake stimulates sympathetic activity of the central nervous system, it is interesting that in former times, salt was considered to arouse passion and desire.

The veneration of salt is perhaps best illustrated by the association of salt with most forms of religion. The earlier gods were worshiped as the givers of the fruits of the earth, including "bread and salt." Salt was an essential component of sacrificial offerings in ancient Egypt, Greece, Rome, and Judaism. In the Roman Catholic Church, salt was introduced as a purifying substance for baptisms in about the fourth century, and it has played a prominent part in certain rituals since.

Social influences of salt: In many instances, the presence of salt seems not only to have determined the site of settlements and their prosperity but also to have influenced the social climate. Where salt was plentiful, such as along the shores of the Mediterranean and the North Sea, societies tended to be free, independent, and democratic, but where it was scarce, "he who controlled the salt controlled the people." For example, in the ancient river valley civilizations of the Nile, in Babylon, Mexico, Peru, and some parts of China, the rulers and priests monopolized salt and used it to manipulate their unfortunate salt-addicted populations.

The immense wealth and prosperity of several empires, including the Chinese and Venetian, were entirely based on salt. The industrial importance of salt remains embedded in the names of certain towns that produced it, for example, Salins in France, Salzburg in Austria, Salzkotten in Prussia, Saltdean in England, Saltcoats in Scotland, and Saltville in Virginia, as well as towns that begin with *Hal* (the Greek for salt), Halle, Hallstadt, and Hallein. Two infamous centers of industrial salt production are mentioned in the Old Testament: Sodom and Gomorrah, which lay at the southern end of the Dead Sea. The citizens of Sodom and Gomorrah indulged in certain sexual habits that were disapproved of in heaven. God, therefore, decided to destroy them. One man named Lot, however, together with his wife and 2 daughters, was led to safety by an angel. They were instructed not to look back at the town they were leaving. Unfortunately, Lot's wife could not resist one backward glance, and she was immediately turned into a pillar of salt. This biblical incident has been depicted in many medieval stained-glass windows, engravings, and paintings.

Salt was often a cause of conflict and at other times influenced the course of a war. In earlier times there were vicious local wars for the possession of salt springs and surface deposits of salt, particularly in Central Europe. The dominance of England in salt export during the 19th century not only had a profound effect on India but also had a decisive effect on the American Civil War, since most of the South's salt requirements had come from England, and the North blockaded the Southern ports.

At the time of the Civil War, the US population was already consuming more salt than any other country, with an average of 50 lb (23 kg) per person per year for all purposes, including preservation of food and preparation of leather. The monthly allowance for a Confederate soldier in 1864 was 1.5 lb (680 g) of salt which, if it were all consumed, would give a minimum of 23 g of salt per day, 4 times the current recommendation of 6 g per day. The South's only sources of salt were well below these needs. Its principal salt-producing areas were in Wilmington, North Carolina, which was lost early in the war, and in Saltville, West Virginia.

The lack of salt severely interrupted the preservation of meat, and its absence in food lowered the morale of the soldiers and the population. Some individuals cornered the market on available salt, which raised its price. The border dividing the Union from the Confederacy stretched for hundreds of miles and made trade between the 2 relatively easy. Blockade running was common along the coast. A profitable run for the North was to transport contraband goods, including salt, to Cuba, where they were picked up by Southern blockade-running ships. A host of illicit traders prospered on both sides. Rhett Butler in *Gone with the Wind* is a prototype of the affluent, glamorous salt blockade–runner. A successful run was an event of major local importance and was reported in the local journals.

General Sherman, who purposely made war against civilians because they supplied the armies he was fighting, was the first to urge the federal authorities to decree that salt be contraband. He asserted that salt was as much a contraband of war as gunpowder. The South, to overcome its grave shortage, used desperate measures. They attempted to obtain salt by boiling seawater at various sites along the west coast of Florida, where nearby forests could supply the necessary fuel. But these sites were regularly destroyed by the North's navy. As regularly, they were back in production within a few days, but the price paid by the South to keep up the production of salt was crippling. The North believed that the destruction of salt stores and the harassment of its production were of equal value in the winning of battles and were worth the cost of the military operations involved. It has been claimed that the lack of salt diverted much of the South's men and money from the first objective of war—to defeat the enemy's army—and thus was an important contribution to the South's defeat.

Dietary salt and blood pressure: According to MacGregor and de Wardener, the earliest comment relating dietary salt to blood pressure came from the Chinese in 1700 BC: "Therefore if large amounts of salt are taken, the pulse will stiffen or harden." It was 3500 years later, in 1836, when Bright of Guy's Hospital in London suggested that the blood pressure of patients with severe renal disease might be raised. Later, another physician at Guy's Hospital noted that high blood pressure also could occur in individuals whose kidneys looked normal. Today, the latter are said to have *essential* or *primary* hypertension, i.e., of unknown cause, which is by far the most common form of high blood pressure,

accounting for 95% of all cases in humans and affecting 10% to 15% of the world's population of 6.2 billion people. Essential hypertension is characterized by a gradual increase in blood pressure with age, so that by age 60, 50% of the population in the Western world has levels that are considered elevated. In the remaining 5% of the hypertensive population, the rise in blood pressure is due to some form of renal or endocrine disease, and the high blood pressure is then known as *secondary* hypertension. In secondary hypertension, the role of dietary salt in causing the blood pressure to rise is now well established. The importance of dietary salt in essential hypertension has been more difficult to discern.

The connection between salt and high blood pressure in patients with essential hypertension was first demonstrated in France in 1904 by Ambard and Beaujard (1). These investigators studied 6 patients with high blood pressure for about 3 weeks. They varied the intake of salt by means of 3 diets: one with very little salt consisted of 2 L of milk per day; the second also had little salt but in addition to milk contained much protein, meat, and eggs; and the third consisted of 2 L of milk plus 2 L of broth containing 10.5 g of salt. The overall salt balance of the patient was measured by estimating the amount of salt excreted in the urine each day. They found that when the diet contained a little salt, more salt was excreted in the urine than was being eaten, so that the patient was in negative sodium balance. The blood pressure fell even when the intake of protein was considerable. (At the time, protein excess was considered the cause of systemic hypertension.) When the diet was high in salt, less salt was excreted in the urine, so that the patient was in positive sodium balance, i.e., retaining salt, and the blood pressure rose even when the protein intake was low. Ambard and Beaujard concluded that they had demonstrated a close relation between salt balance and blood pressure.

During the following 20 years, salt deprivation was used to lower blood pressure, mainly in patients with renal disease, but with poor results. The idea that there was a connection between hypertension and salt was discredited, and the "protein intoxication" fear dominated the scene well into the 1930s. In 1922, Allen and Scherril described the effect of a low-salt diet in 180 patients with severe essential hypertension who were given a normal protein intake (1). The blood pressure returned to normal in 19%. In 42%, the fallen blood pressure and the relief of symptoms were sufficient to be regarded as therapeutically successful. Complete failure occurred in 30%. These authors concluded that essential hypertension was a "salt nephritis." Houghton, writing the same year, discussed all the effects of salt reduction in several forms of hypertension and proposed that a rise in blood pressure is "a tertiary condition of which the immediate cause is a larger salt intake than the damaged kidneys can excrete." This is a very modern view.

Despite the work of Ambard and Beaujard, Allen and Scherril, Houghton, and a few others, the connection between salt intake and hypertension continued to be denied (1). The position was finally clarified by Kempner in 1948. He had devised a diet with which to treat hypertension that was low in fat, contained 20 g of protein, and contained <0.5 g of salt per day. It consisted of plain rice and fruit. Kempner was most interested in the relatively low protein content of his diet and thus was reluctant to admit that it might be the low salt content of the diet that lowered blood pressure. He attributed such an assertion to others who used his diet. It is ironic that Kempner is now remembered as the person who demonstrated beyond any shadow of a doubt that high blood pressure can often be lowered by a low-salt diet. Kempner's diet was so low in salt that the 24-hour urinary excretion of salt at the end of 2 months usually fell to <0.25 g.

Kempner published the effect of his diet on 500 patients with essential hypertension. The article is illustrated by charts showing relentless falls in blood pressure, chest radiographs showing pronounced reductions in heart sizes, electrocardiograms showing gross abnormalities reverting to normal, and photographs of damaged retinae that dramatically improved. There is no doubt that Kempner's rice diet achieved remarkable and sustained results. He made no mention, however, of how difficult it was to get patients to follow his rice diet nor of the complications associated with such severe and rapidly induced reductions in salt intake. One reason he was so successful using his diet when others failed was that he collected all the urine excreted each day from the patients so that by the time he saw them in the ward he knew how much salt they were excreting and therefore how much they had eaten. Kempner's reactions when they had erred were such that the patients were unlikely to err again. His use of salt restriction at this time was the only therapeutic maneuver that lowered blood pressure.

Not surprisingly, when oral diuretics were developed in the mid-1950s, the increased excretion of salt they induced through the kidneys was considered a satisfactory alternative to a low-salt diet and a much more convenient way of dealing with the habitual high consumption of salt. With the increasing realization since the 1970s that diuretics have adverse consequences, the use of more moderate dietary salt to control high blood pressure in essential hypertension has been revised by reducing salt intake to 3 to 6 g of salt per day. Numerous trials have shown that such reductions cause a fall in blood pressure, which is greatest in the elderly and in those with the highest blood pressure.

A link between salt and blood pressure also can be demonstrated by measuring the small changes in blood pressure that are rapidly induced by an abrupt change in salt intake or salt output, for example, an intravenous infusion of saline or the administration of the diuretic. Those individuals in whom this causes the least change in arterial pressure are termed *salt resistant*, whereas those in whom they induce larger changes are referred to as *salt sensitive* and are considered by some to be more likely to develop hypertension later in life. There is little evidence, however, that the immediate response of the blood pressure to such sudden, drastic changes in salt status indicates how the blood pressure of an individual responds to a lifetime's exposure to a high-salt diet.

The effect of a reduction in dietary salt intake on the arterial pressure of normal subjects has been measured in newborn babies, school children, and adults. Nonhuman animal studies have shown that young animals are much more sensitive to the level of dietary salt intake than adults and that even a transient rise in intake early in life may increase their response to a high intake later in life. In a large study of 750 children, a 2-g reduction in salt intake to an intake of 7 g a day induced a significant

fall in blood pressure after 6 months. In a similar study in 32 adults (average age, 40 years), mean reduction of urinary salt excretion from 9 to 4 g per day caused a significant fall in blood pressure at 12 weeks, and the fall in pressure was correlated with the fall in salt excretion. In normal circumstances, salt excretion is almost the same as salt intake. In a study of adults aged 60 to 78 years, a reduction in salt intake from 10 to 5 g per day for 4 weeks reduced systolic pressure by 8 mm Hg and diastolic pressure by 4 mm Hg, which is similar to that found in trials with blood pressure–lowering drugs. The extent of the fall in blood pressure was the same whether the subject started with a high or a normal blood pressure.

Severe increases in salt intake for a few days have little effect on normal blood pressure. In young adults, 28 g of salt per day was required to cause a rise in blood pressure. In subjects >50 years of age, however, only 20 g per day for a few days was necessary to cause a rise in blood pressure. It appears, therefore, that the effect of a sudden rise in dietary salt intake on normal blood pressure during a person's life varies and is most pronounced in the very young and after age 50.

A well-documented connection between hypertension and dietary salt intake has been demonstrated in normal dogs, rabbits, rats, baboons, and chimpanzees. A study done in 1951 found that the substitution of a 1% salt solution for drinking water produced hypertension in the chicken, rat, and rabbit. It was established that whatever experimental method was used to induce secondary hypertension (e.g., by partially obstructing a renal artery), it was facilitated by increasing the salt intake and prevented by salt restriction. The experiments in chimpanzees strongly reinforced the proposal that essential hypertension is due to the prevailing high intake of salt. Chimpanzees normally consume a diet low in salt, but when their salt intake increases to that of present-day humans, they develop hypertension. This similarity is made closer by the finding that, again like humans, a number of chimpanzees did not develop high blood pressure on the high-salt diet. It was very noticeable that the rise in pressure was gradual and that blood pressure was still rising 18 months after they started eating the high-salt diet. Furthermore, upon returning to a diet that contained <0.5 g of salt per day, the blood pressure fell to its original level.

There have been nearly 40 accounts of certain primitive populations in which blood pressure did not rise with age—in other words, they did not have essential hypertension. In most, dietary intake of salt was <3 g per day; in a few, it was <1 g per day; and in one, it was about 0.05 g per day. At the other end of the scale, there have been studies among several Japanese and Portuguese communities with a high prevalence of hypertension. In one, the salt intake averaged 26 g per day. In between are the bulk of westernized societies that consume 7 to 12 g per day (average, 10 g). The connection between salt intake and hypertension in these intermediate populations is evident but more difficult to discern, mainly because of the narrow range of salt intake.

The Yanomamo Indians are probably the most primitive native tribe in the world. They live in about 100,000 square miles along the border between Venezuela and Brazil. Approximately 18,000 individuals are scattered through the Amazon rain forest in about 200 villages, with 40 to 200 persons in each. They have been described as seminomadic, "slash-and-burn" agriculturists living on a diet of locally produced crops and game supported by wild fruits and insects. Their staple foods are cooked bananas and manioc. Most villages have little access to salt, refined sugar, alcohol, milk, or dairy products. In one group of 206 persons aged 20 to 50 years, which comprised all the adults from 3 villages, the mean 24-hour urinary excretion of salt was 0.5 g per day, with a potassium excretion of 3 g per day. The mean weight of the men (50 kg) was about the same as that of chimpanzees. Their blood pressure was much lower than that found in Western populations, and there was no rise in blood pressure with increasing age. Their blood pressure, just like that of the Western world, is approximately 90/60 mm Hg at birth, and that is their blood pressure their entire lives. The Yanomamos probably represent the ultimate human example of the importance of salt on blood pressure.

Although numerous studies comparing a wide range of communities have confirmed a significant relation between salt intake (measured as 24-hour salt excretion) and blood pressure, one obstacle has bothered and continues to bother a great many researchers: within a single community, there is no relation between the blood pressure and salt intake of individuals. There are many reasons for this apparent lack of correlation. Blood pressure varies from day to day within an individual and also depends on the manner in which the blood pressure is measured. More important is the fact that while the spread of the average amount of salt ingested by individuals of a single community is relatively narrow, the day-to-day fluctuations in salt ingested and excreted by each individual in any 24-hour period may vary enormously. Day-to-day variations in 24-hour salt excretion of 3 to 18 g per day have been recorded. Such variations depend on the type of food eaten the previous day and its salt content. To obtain an accurate estimate of any one individual's average salt excretion, it is necessary to measure the salt excretion on >5 occasions, which is not practical when studying large numbers of people. Such very large methodological difficulties obviously mask the detection of differences between subjects. These facts have been appreciated since 1960.

The relation of blood pressure to salt intake was extensively studied by Dahl (1). Over a number of years, he and his associates measured the blood pressure and the 24-hour urinary excretion of salt in Alaskan Eskimos, Marshall Islanders in the Pacific, and employees at the Brookhaven Laboratory in the USA, where Dahl worked. When the results were plotted, the correlation between the average daily salt intake and the prevalence of hypertension in these different centers was excellent. The Eskimos, whose salt intake appeared to be 4 g per day, had no hypertension. Fukuda's investigations in Japan disclosed that the Japanese had the highest salt intake and the highest prevalence of hypertension, and the other 3 were in between. The implication was that, though the relation between salt intake and blood pressure was not evident within the individuals in most populations, salt intake controlled the blood pressure.

Dahl also studied the employees at Brookhaven. He first studied their use of salt at the table where "the salt shakers were ubiquitously available." He found that the personnel could be classified into 3 groups: 1) those who had a low intake of salt who did not add and had never added salt to food; 2) those who had

an average intake of salt who added salt to food only if, after first tasting it, they found it insufficiently salty for their palate; and 3) those who had a high intake of salt, who were in the habit of adding salt to food without first tasting its degree of saltiness. It turned out that the incidence of hypertension was significantly different from a random distribution. Though the mean blood pressures of the 3 groups were not significantly different, among those classified as having been on a low intake throughout their lives, significantly fewer persons had high blood pressure than among those classified as having been on a high intake.

High blood pressure in African Americans: African Americans have the highest prevalence of high blood pressure in the world. The prevalence of high blood pressure is nearly twice as high among African Americans than in Caucasian Americans (38% vs 20%) and 2 to 4 times higher than in West Africans. The degree of hypertension appears to correlate with darkness of skin color. The blood pressure of African Americans also is more sensitive to increases in salt intake than that of American whites, and they retain an intravenous load of salt far longer than whites. Conversely, it is easier to lower the blood pressure of African Americans with a diuretic. All of these facts indicate that African Americans have an enhanced ability to retain salt or a diminished ability to get rid of a high-salt intake.

A hypothesis has been put forward to explain the high prevalence of hypertension in African Americans: that the process of enslavement decimated those who were least able to conserve salt so that the survivors were individuals who were best able to conserve salt. Between 1500 and 1800, >12 million black people were transported against their will from the west coast of Africa to the Western Hemisphere. Most went to South America. But 6% of the total, estimated to be about 430,000 slaves, ended up in North America. Many came from very low-salt areas in West Africa, such as the sub-Saharan Savanna. After capture, slaves were force-marched 100 to 200 miles to the coast by African slave handlers. There they were confined to long, crowded huts known as barracoons to wait several weeks or months for the ships to take them away. The death rate from the point of capture to the coast was about 10%, and another 12% died in the barracoons. Conditions on board ship were terrible, and on average 15% died during the 2 months of the crossing. Another 5% died while waiting to be sold in the USA, and a further 10% died in the subsequent 2 years when they were being "seasoned" to their new environment. Thus, on average, only 50% of those captured survived >2 years. The most common cause of death was illness associated with loss of salt and water. Slaves were exposed to heat and excessive sweating during the forced marches to the coast and the incarceration in the unventilated barracoons and ships' holds. During the sea voyage, vomiting due to seasickness was common. Diarrhea was always rife, and the predominant cause of death was some form of diarrhea.

Death left a dwindling number of survivors, but death was not random. The hypothesis suggests that having kidneys that had a well-developed ability to retain salt would have increased the chances of surviving. As this process of attrition by various forms of dehydration was repeated over a period of 1 to 3 years, the cumulative effect would be highly selective. According to the hypothesis, it is this selective survival of genes responsible for an increased ability to retain salt that is now responsible for the exceptionally high prevalence of hypertension in African Americans.

Mechanism for salt's effect on blood pressure: The lack of an obvious mechanism whereby salt intake controls blood pressure has been one factor that has delayed acceptance of their relation. There is evidence that in essential hypertension in humans, in secondary hypertension in humans associated with overt renal disease, and in hereditary hypertension in rats, the kidney has difficulty excreting salt, and this sets in motion a chain of events that causes blood pressure to rise. This evidence is based on 2 types of observations: those that show that the rise in blood pressure is due to an abnormal kidney and those that demonstrate that the kidney has a diminished ability to excrete salt. However, there is a chicken-and-egg complication in this explanation. When the blood pressure rises, it causes widespread changes, particularly in the kidney, which it sometimes even destroys. Therefore, the evidence that is pertinent to the search for the initial cause of the rise in pressure has to be distinguished from the changes produced by the high blood pressure itself. When possible, this distinction is most easily made by studying the persons or animals that are going to develop hypertension when they are young, before they develop hypertension.

Kidney cross-transplant experiments have provided confirmation that the initiating trigger that causes blood pressure to rise is in the kidney. Donor kidneys came from either a prehypertensive hypertensive-strain rat or from a normotensive control animal. When a kidney from a prehypertensive hypertensive-strain rat was transplanted into a control normotensive rat, blood pressure rose. When a kidney from a control rat was transplanted into a prehypertensive hypertensive-strain rat, blood pressure did not rise. When a kidney from a normotensive rat was placed into a hypertensive strain that had already developed high blood pressure, blood pressure came down. These experiments demonstrate that the blood pressure follows the kidney.

Similar results have been obtained in humans with essential hypertension. In 6 black patients with terminal renal failure due to prolonged essential hypertension, the blood pressure fell to normal and remained normal for many years after receiving a kidney from a young, normotensive donor. In another investigation, researchers measured the blood pressure of the parents of the kidney donor, as well as that of the recipients. They found that patients who received a kidney from a donor whose family had high blood pressure needed significantly more blood pressure–lowering therapy than those who received a kidney from a donor whose family had normal blood pressure.

There is some evidence that normotensive children of parents with essential hypertension have difficulty excreting salt. For instance, compared with control subjects, the administration of a salt solution intravenously at a certain rate to normotensive first-degree relatives of patients with essential hypertension led to a rise in blood pressure and reduced salt excretion. An increase in salt intake to 16 g per day for 7 days caused an increase in blood pressure in normotensive offspring of hypertensive patients but did not raise the blood pressure of normotensive offspring of normotensive parents. These observations suggest that though the kidney in essential hypertension looks normal, it has an inherited impaired ability to excrete salt. It is now evident that many intrinsic renal functional abnormalities are present. There

are disturbances of kidney blood flow and of several locally produced kidney hormones and other substances that control salt excretion. Thus, the rise in blood pressure in essential hypertension depends on the magnitude of the excess salt intake; the type, severity, and combination of intrinsic renal abnormalities that impair the kidney's ability to excrete salt; and the number of years the individual has suffered from this conflict. Exactly how the kidney's difficulty to excrete salt raises the blood pressure is not known.

Commercial reasons for producing high-salt food: The above evidence indicates a very strong connection between salt intake and blood pressure. Why, then, is so much salt continually added to foods? The first reason is taste. Tomato juice without salt is virtually intolerable, for example. The food industry is more than happy to agree in public that taste is the major reason why it adds salt to food. The other 2 reasons, however, are entirely commercial; for most foods, these are the real reasons the food industry wants salt intake to remain high. One is that the salt content of food is an important determinant of the amount of water the food contains and therefore of its weight. Salt increases the weight of food at very little cost. For instance, if the salt content of sausages is increased from 0.5% to 2.5%, which is the normal concentration of salt in sausages, their water content can be increased by approximately 20%. Far less salt could be added if other flavors were substituted, but since this would reduce the weight of the sausage, consumers would expect the price to fall. It is probably also true that some of the cheapest processed food, which consists predominantly of pure animal fat and mechanically recovered meat, would be fairly tasteless without salt. The second commercial reason is that salt increases thirst. In most temperate climates, the body needs only about a liter of fluid a day. If, however, the consumption of salt is increased, the salt concentration of the body tends to rise, which stimulates thirst and therefore the amount one drinks. There is thus a direct relation between salt intake and fluid intake. It is not surprising that in pubs there are often free supplies of salted peanuts and potato chips and that many of the soft drink manufacturers, some of whom also make alcoholic drinks, own companies that specialize in the manufacture of highly salted snacks. It is said that these companies have calculated that if salt intake were to be reduced, they would lose hundreds of millions of dollars in sales of soft drinks!

The US salt extractors and salt manufacturers finance a public relations body known as the Salt Institute. This institute appears to be an independent body giving advice about salt but in reality gives a one-sided story supporting the high salt content of processed food. The institute propagates the view that there is considerable debate within the medical and scientific community as to whether any relation exists between hypertension and sodium intake in the general population and that a decrease in sodium intake may result in a decrease in blood pressure for some, an increase in blood pressure for others, and no significant change in blood pressure for most. This view is very reminiscent of that taken by the tobacco industry for many decades regarding the danger (or lack thereof) of cigarettes.

The Salt Institute, which seemed to know about the Intersalt study (the worldwide investigation on the relation of salt excretion to blood pressure) before its publication, turned the study on its head and interpreted it in a way opposite that of the authors by saying that salt intake had no relation to blood pressure. The institute's attempts to discredit the Intersalt study have continued unrelentingly.

The Salt Institute, a large snack company, and the US Dairy Council have been heavily involved in suggesting that what really raises blood pressure is not a high salt intake but a low calcium intake and that consuming more calcium (e.g., milk) would solve the blood pressure problem. Giving calcium to patients with high blood pressure, however, has not lowered it, and indeed there is little to no relation between calcium intake and blood pressure in different populations. The Salt Institute then argued that a very high calcium intake lowered blood pressure in individuals who were already on a high salt intake. This has not proven to be the case. Much more troublesome for the milk industry is the recent evidence that a high salt intake is an important aggravating factor in bone demineralization and that reducing salt intake is likely to have a greater beneficial effect on bone density than increasing calcium intake. The food industry's next rather rash maneuver was to assert that a moderate reduction in salt intake might be dangerous. Close analysis of the study cited in support failed to back up this claim.

Decreasing salt intake: Since there is little doubt that increased salt intake increases blood pressure, what steps can we take to decrease the intake of salt? There are at least 3: 1) *Do not add salt at the table*. It is not impolite not to pass the salt shaker! Also, sauces that are added to food or added at the table, such as tomato ketchup, are usually very high in salt. Adding salt at the table is essentially a habit. This was clearly demonstrated in a study in an Australian canteen in which the hole in the saltcellar was reduced. As a result, the habitual unthinking number of shakes delivered only half the quantity of salt. No one noticed any difference. 2) *Stop adding salt when cooking*. This is more difficult, as it requires the agreement of the person who does the cooking in the household. At first, the food will taste bland. Two to 4 weeks later, however, as the salt taste receptors in the mouth become more sensitive to the taste of salt in the usual high concentrations, the taste of salt becomes more unpleasant. It is the same as giving up sugar in tea or coffee—initially it is difficult, but later the taste of sugar in tea or coffee is disgusting. Salt is often added inadvertently; all stock cubes, gravy brownings, soy sauce, and prepared mustard contain large amounts of salt and should be avoided. 3) *Avoid manufactured foods or processed foods that have salt added*. This is by far the most difficult step, because many processed foods are not labeled with their salt content, and if they are labeled, the labels tend to be confusing. Buying as much fresh food as possible or buying foods with <0.1 g of sodium per 100 g of food is useful, but few processed foods achieve such low concentrations.

Measuring salt intake: The simplest way to measure salt intake is as grams of salt a day. Because some of the sodium salts we eat are not in the form of sodium chloride (e.g., sodium bicarbonate), it is more correct scientifically to talk about sodium intake. Food labels in the supermarket will not, therefore, give the salt content or equivalent salt content of the food. Instead, they will give the sodium content of food, usually in grams or fractions of a gram per 100 g of food. To convert the content of sodium in food to sodium chloride (salt), it is necessary to mul-

tiply by approximately 2.5, for 1 g of sodium is equivalent to 2.5 g of salt. To calculate the amount of salt that is consumed when eating a particular processed food, it is necessary to multiply the concentration of salt in the food by its weight. For instance, if a prepared meal has a sodium concentration of 1 g of sodium per 100 g of food, it contains $1 \times 2.5 = 2.5$ g of salt per 100 g of food. If the whole meal weighs 250 g, the total amount of salt it contains is 2.5 (g of salt) $\times$ 2.5 (250 g) = 6.25 g of salt. This one prepared meal, therefore, contains the total current recommended daily intake of salt.

Labeling the amounts of salt in food as grams of sodium per 100 g of food makes the content of salt seem deceptively small. It would be much better to adopt a food labeling system in milligrams and express the value as a salt equivalent. For instance, an average supermarket loaf of bread contains 0.5 g of sodium per 100 g, i.e., 500 mg of sodium per 100 g of bread, which is equivalent to $500 \times 2.5 = 1250$ mg (1.25 g) of salt per 100 g. One slice of bread weighs approximately 40 g. Therefore, each slice of bread contains 0.4×1250 mg, which is 500 mg of salt per slice. If the recommended dose of salt intake is 6 g, 1 slice of bread is equivalent to one twelfth of the recommended intake, and 4 slices take up to 30% of the recommended intake.

The labeling system in the USA is cumbersome, to say the least. The packet is labeled with how eating 1 portion of that food contributes to the recommended dietary intake (6 g of salt per day). An average packet of salted potato chips contains 2 g of salt, which would account for 30% of the recommended daily salt intake. The idea behind this food labeling system is that consumers can then add up all of these percentages and work out whether their salt intake for the day is above or below the recommended intake.

Foods with a low salt content include all fresh and frozen vegetables. Vegetables in tin cans generally have salt added. Fresh meat is low in salt. All uncooked pasta, rice, olive oil, rapeseed oil, unsalted nuts, fruit juices, tea, coffee, and most alcoholic drinks are low in salt. In contrast, the foods that have a high salt content include meat products (e.g., bacon, ham, cured meat, canned meat, sausages, paté), smoked fish and fish in tin cans, instant noodles and soups, canned or packet soups, stock cubes, gravy brownings, yeast extracts, meat extracts, vegetable juices, and soy sauce. Most fast foods contain large amounts of salt as well as saturated fat. A hamburger with french fries generally contains approximately 5 g of salt.

In conclusion, salt and blood pressure go together. The more salt we take in, the higher our blood pressure will be. Most strokes are directly related to blood pressure, and, therefore, the easiest way to decrease the frequency of stroke is to decrease blood pressure, and one way to do that is to decrease salt intake. Any change in our diet takes time to get used to, and this particularly applies to reducing salt intake. It will take at least a month for the salt taste receptors to adjust to a lower salt concentration, but they will then become more sensitive, and it will be possible to distinguish the natural and more enjoyable taste of food.

Thank you, Drs. MacGregor and de Wardener, for producing such a fine book.

NEW GUIDELINES FOR TREATING HIGH BLOOD CHOLESTEROL IN ADULTS

The executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel (Adult Treatment Panel III [ATPIII]) appeared in the May 16, 2001, issue of *JAMA* (2). The first guidelines appeared in 1988 and the second in 1993, so the present guidelines are the first to appear in 8 years. The 13-page executive summary is based on the comprehensive ATPIII document, a >200-page report that includes numerous tables and >800 references and in which the NCEP panel thoroughly evaluated current scientific information on cholesterol, applying a rigorous evidence-based framework, and outlined the clinical and scientific rationale for the guidelines and recommendations. This report is available at http://www.nhlbi.nih.gov/guidelines/cholesterol/index.htm.

The ATPIII report has several new features. It

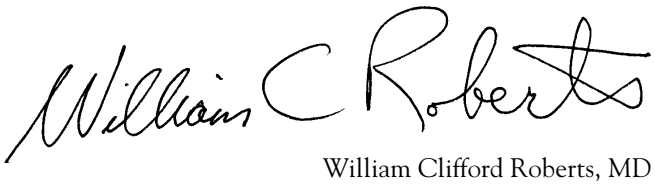
- Places persons with diabetes mellitus without coronary artery disease—most of whom have multiple risk factors—at the risk level of CHD risk equivalent
- Uses the Framingham projections of 10-year absolute CHD risk (i.e., the percent probability of having a CHD event in 10 years) to identify patients with ≥2 risk factors for more intensive treatment
- Identifies persons with the metabolic syndrome as candidates for intensified therapeutic lifestyle changes
- Identifies optimal low-density lipoprotein (LDL) cholesterol as <100 mg/dL; raises the definition of low high-density lipoprotein (HDL) cholesterol from <35 mg/dL to <40 mg/dL; and lowers the definition of elevated triglyceride level to ≥150 mg/dL
- Recommends a complete lipoprotein profile (total, LDL, and HDL cholesterol and triglycerides) as the preferred initial test rather than screening for total cholesterol and HDL alone
- Encourages the use of plant stanols-sterols and viscous (soluble) fiber as therapeutic dietary options to enhance lowering of LDL cholesterol
- Presents strategies for promoting adherence to therapeutic lifestyle changes and drug therapies
- Recommends treatment beyond LDL lowering for persons with triglycerides ≥200 mg/dL

Among patients without CHD, emphasis is placed on prospectively estimating absolute risk. This is done by providing points for various age groups, for various total cholesterol levels, for smoking or nonsmoking, for HDL levels, and for various systolic blood pressure levels. Points from these 5 categories are then added up to determine percentage with likely coronary event within 10 years. Separate 10-year risk tables are provided for both men and women. Calculations from these tables are relatively simple and can be done in probably a minute.

Another important feature of the ATPIII executive summary is its emphasis on the metabolic syndrome, defined as abdominal obesity (waist circumference >40" in men and >35" in women); triglycerides ≥150 mg/dL; HDL in men <40 and in women, <50 mg/dL; blood pressure ≥130/≥85 mm Hg; and fasting glucose ≥110 mg/dL. The metabolic syndrome is obviously extremely common in the USA. In addition to the triglyceride levels being elevated, the HDL cholesterol is usually depressed, and the LDL cholesterol molecule is usually small and dense. The

insulin levels are increased, and that is what gave rise to the term "insulin-resistance syndrome." Other non-HDL–related recommendations in ATPIII include incorporating triglyceride levels into treatment strategies when they exceed 200 mg/dL and recognizing that in some patient populations treatment specifically designed to increase HDL levels is appropriate.

These guidelines should increase the number of US patients receiving statin drugs from around 13 million to possibly 36 million. My criticism of the guidelines is that they have to do with decreasing risk of atherosclerotic events rather than focusing on preventing and arresting the atherosclerotic process. Because atherosclerosis is familial only about 0.2% of the time, cholesterol levels must be much lower than recommended in these guidelines to prevent the process. Pediatricians do not talk about decreasing the risk of measles, mumps, whooping cough, or polio; they talk about preventing the disease. I think that we should approach atherosclerosis in the same way.



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1. MacGregor GA, de Wardener HE. *Salt, Diet and Health: Neptune's Poisoned Chalice: The Origins of High Blood Pressure*. Cambridge, UK: Cambridge University Press, 1998.
2. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA* 2001;285:2486–2497.